

Applicant : Paul G. Yock, et al.  
Appl. No. : 10/776,037  
Examiner : Marvich, Maria  
Docket No. : 13854.4004

### **Amendments to the Claims**

In accordance with 37 C.F.R. 1.173(b)(2), the following claims are changed or added by this amendment:

1. (Twice Amended) A method of locally administering an active agent to a host, said method comprising:

retroinfusing said agent into a vascular vessel of said host under conditions sufficient for the agent or a fluid delivery vehicle thereof to produce a disruption in said vessel and for said agent to enter an interstitial space of said host through said disruption so that said agent is locally administered to said host, wherein said disruption comprises a passageway created in a wall of said vessel.

2. The method according to claim 1, wherein said vessel is a vein.

3. The method according to claim 1, wherein said retroinfusing comprises providing stress to said vascular vessel at a site at least proximal to said interstitial space.

4. The method according to claim 1, wherein said method further comprises using depot means.

5. The method according to claim 1, wherein said method further comprises administration of energy to said vessel.

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6. The method according to claim 1, wherein said interstitial space is myocardial interstitial space.

7. The method according to claim 3, wherein said retroinfusing comprises administering said agent at a pressure sufficient to produce at least a mechanical stress on said vessel.

8. (Twice Amended) A method of locally administering an active agent to a host, said method comprising:

retroinfusing said agent into a vein of said host under conditions sufficient for the agent or a fluid delivery vehicle thereof to produce a disruption in said vein [vessel] and for said agent to enter an interstitial space of said host through said disruption so that said agent is locally administered to said host, wherein said disruption comprises a passageway created in a wall of said vein.

9. The method according to claim 8, wherein said retroinfusing comprises administering said agent at a pressure sufficient to produce at least a mechanical stress on said vein.

10. The method according to claim 8, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.

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11. The method according to claim 8, wherein said method further comprises producing [inflammation] inflammation in said vein.

12. The method according to claim 8, wherein said interstitial space is myocardial interstitial space.

13. The method according to claim 9, wherein said pressure is sufficient to at least distend said vein.

14. The method according to claim 9, wherein said pressure is sufficient to disrupt said vein.

15. (Twice Amended) A method of locally administering an active agent to a host, said method comprising:

retroinfusing said agent into a vein of said host with a catheter and at a pressure sufficient for the agent or a fluid delivery vehicle thereof to produce a disruption in [on] said vein such that said agent enters an interstitial space proximal to the vein through said disruption, wherein said disruption comprises a passageway created in a wall of said vein;  
whereby said agent is locally administered to said host.

16. The method according to claim 15, wherein said pressure is sufficient to at least distend said vein.

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17. The method according to claim 16, wherein said pressure is sufficient to disrupt said vein.

18. The method according to claim 16, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.

19. The method according to claim 16, wherein said method further comprises producing [inflammation] inflammation in said vein.

20. The method of claim 1 wherein said agent comprises cells.

21. The method of claim 1 wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.

22. The method of claim 1 wherein said agent comprises therapeutic nucleic acids.

23. The method of claim 22 wherein the therapeutic nucleic acids comprise at least one gene.

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24. The method of claim 1 wherein said agent comprises a dye or an imaging agent.

25. The method of claim 1 wherein said retroinfusion is performed at a pressure of at least 50 mm Hg.

26. The method of claim 1 wherein said retroinfusion is performed at a pressure of at least 60 mm Hg.

27. The method of claim 1 wherein said retroinfusion is performed at a pressure of at least 1000 mm Hg.

28. The method of claim 5 wherein the energy administered is selected from the group consisting of ultrasound, heat, electroporation and radio frequency energy.

29. The method of claim 3 wherein said stress is chemical stress.

30. The method of claim 1 wherein said vessel is an artery.

31. The method of claim 2 wherein said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruptions in the venous branches.

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32. The method of claim 1 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.

33. The method of claim 32 wherein at least one upstream branch of said vessel is occluded.

34. The method of claim 2 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.

35. The method of claim 34 wherein said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruption in the venous branches.

36. The method of claim 1 wherein said pressure is sufficient to at least distend said vessel.

37. (Twice Amended) A method of locally administering an active agent to a host, said method comprising:

retroinfusing a fluid into a vascular vessel of said host under conditions sufficient for the fluid to produce a disruption in said vessel and infusing said agent into an interstitial space of said host through said disruption and locally administering said agent to said host through said disruption, wherein said disruption comprises a passageway created in a wall of said vessel.

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38. The method according to claim 37, wherein said vessel is a vein.

39. The method according to claim 37, wherein said retroinfusing comprises providing stress to said vascular vessel at a site proximal to said interstitial space.

40. The method according to claim 37, wherein said method further comprises using depot means.

41. The method according to claim 37, wherein said method further comprises administration of energy to said vessel.

42. The method according to claim 37, wherein said interstitial space is myocardial interstitial space.

43. The method according to claim 39, wherein said retroinfusing comprises administering said fluid at a pressure sufficient to produce at least a mechanical stress on said vessel.

44. (Twice Amended) A method of locally administering an active agent to a host, said method comprising:

retroinfusing a fluid into a vein of said host under conditions sufficient for the fluid to produce a disruption in said vein and infusing said agent into an interstitial space of said

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host through said disruption so that said agent is locally administered to said host, wherein said disruption comprises a passageway created in a wall of said vein.

45. The method according to claim 44, wherein said retroinfusing comprises administering said fluid at a pressure sufficient to produce at least a mechanical stress on said vein.

46. The method according to claim 44, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.

47. The method according to claim 44, wherein said method further comprises producing inflammation in said vein.

48. The method according to claim 44, wherein said interstitial space is myocardial interstitial space.

49. The method according to claim 45, wherein said pressure is sufficient to at least distend said vein.

50. The method according to claim 45, wherein said pressure is sufficient to disrupt said vein.



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51. (Twice Amended) A method of locally administering an active agent to a host, said method comprising:

retroinfusing a fluid into a vein of said host with a catheter and at a pressure sufficient for the fluid to produce a disruption in said vein and infusing said agent into an interstitial space proximal to the vein through said disruption, wherein said disruption comprises a passageway created in a wall of said vein;

whereby said agent is locally administered to said host.

52. The method according to claim 51, wherein said pressure is sufficient to at least distend said vein.

53. The method according to claim 52, wherein said pressure is sufficient to disrupt said vein.

54. The method according to claim 52, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.

55. The method according to claim 52, wherein said method further comprises producing inflammation in said vein.

56. (Twice Amended) A method of locally administering an active agent to a host, said method comprising:

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retroinfusing said agent into a vascular vessel of said host under conditions sufficient for the agent or a fluid delivery vehicle thereof to produce at least a mechanical stress on said vessel, which stress facilitates the transport of said agent through the wall of said vessel so that said agent is locally administered to said host by producing a disruption in the wall of said vessel, wherein said disruption comprises a passageway created in the wall of said vessel.

wherein said method further comprises administration of energy to said vessel.

57. (Amended) The method according to claim 56, wherein said retroinfusing comprises administering the agent or the fluid delivery vehicle thereof at a pressure sufficient to at least distend said vessel.

58. (Amended) The method according to claim 56, wherein said retroinfusing comprises administering the agent or the fluid delivery vehicle thereof at a pressure sufficient to disrupt said vessel.

59. The method according to claim 56, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.

60. The method according to claim 56, wherein said method further comprises producing inflammation in said vessel.

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61. The method of claim 56 wherein said vessel is an artery.

62. The method of claim 58 wherein said vessel is a vein, and said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruptions in the venous branches.

63. The method of claim 56 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.

64. The method of claim 63 wherein at least one upstream branch of said vessel is occluded.

65. The method of claim 58 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.

66. The method of claim 65 wherein said vessel is a vein, and said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruption in the venous branches.

67. (Twice Amended) A method of locally administering an active agent to a host, said method comprising:

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retroinfusing said agent into a vascular vessel of said host under conditions sufficient for the agent or a fluid delivery vehicle thereof to at least distend said vessel, which distention facilitates the transport of said agent through the wall of said vessel so that said agent is locally administered to said host by producing a disruption in the wall of said vessel, wherein said disruption comprises a passageway created in the wall of said vessel, wherein said method further comprises administration of energy to said vessel.

68. The method according to claim 67, wherein said retrofusing comprises administering said fluid at a pressure sufficient to produce at least a mechanical stress on said vessel.

69. (Amended) The method according to claim 67, wherein said retroinfusing comprises administering the agent or the fluid delivery vehicle thereof at a pressure sufficient to disrupt said vessel.

70. The method according to claim 67, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.

71. The method according to claim 67, wherein said method further comprises producing inflammation in said vessel.

72. The method of claim 67 wherein said vessel is an artery.

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73. The method of claim 69 wherein said vessel is a vein, and wherein said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruptions in the venous branches.

74. The method of claim 67 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.

75. The method of claim 74 wherein at least one upstream branch of said vessel is occluded.

76. The method of claim 69, wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.

77. The method of claim 76, wherein said vessel is a vein, and wherein said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruption in the venous branches.

78. (Twice Amended) A method of locally administering an active agent to a host, said method comprising:

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retroinfusing a fluid into a vascular vessel of said host under conditions sufficient for the fluid to produce a mechanical stress in said vessel, which stress facilitates the transport of said agent through a wall of said vessel so that said agent is locally administered to said host by producing a disruption in the wall of said vessel, wherein said disruption comprises a passageway created in the wall of said vessel,

wherein said method further comprises administration of energy to said vessel.

79. The method according to claim 78, wherein said vessel is a vein.

80. (Amended) The method according to claim 78, wherein said retroinfusing comprises administering the fluid at a pressure sufficient to at least distend said vessel.

81. (Amended) The method according to claim 78, wherein said retroinfusing comprises administering the fluid at a pressure sufficient to disrupt said vessel.

82. The method according to claim 78, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.

83. The method according to claim 78, wherein said method further comprises producing inflammation in said vessel.

84. The method of claim 78 wherein said vessel is an artery.

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85. The method of claim 78 wherein said vessel is a vein, and said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruptions in the venous branches.

86. The method of claim 78 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.

87. The method of claim 86 wherein at least one upstream branch of said vessel is occluded.

88. The method of claim 81 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.

89. The method of claim 88 wherein said vessel is a vein, and said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruption in the venous branches.

90. (Twice Amended) A method of locally administering an active agent to a host, said method comprising:

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retroinfusing a fluid into a vascular vessel of said host under conditions sufficient for the fluid to at least distend said vessel, which distention facilitates the transport of said agent through the wall of said vessel so that said agent is locally administered to said host by producing a disruption in the wall of said vessel, wherein said disruption comprises a passageway created in the wall of said vessel,

wherein said method further comprises administration of energy to said vessel.

91. The method according to claim 90, wherein said vessel is a vein.

92. (Amended) The method according to claim 90, wherein said retroinfusing comprises administering the fluid at a pressure sufficient to disrupt said vessel.

93. The method according to claim 90, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.

94. The method according to claim 90, wherein said method further comprises producing inflammation in said vessel.

95. The method of claim 90 wherein said vessel is an artery.

96. The method of claim 92 wherein said vessel is a vein, and said retroinfusion comprises disruption of venous branches upstream of the site of administration for said



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agent to enter an interstitial space of said host through the disruptions in the venous branches.

97. The method of claim 90 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.

98. The method of claim 97 wherein at least one upstream branch of said vessel is occluded.

99. The method of claim 92, wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.

100. The method of claim 99, wherein said vessel is a vein, and wherein said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruption in the venous branches.

101. The method according to claim 56, wherein said energy administered is selected from the group consisting of ultrasound, heat, electroporation and radio frequency energy.

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102. The method according to claim 67, wherein said energy administered is selected from the group consisting of ultrasound, heat, electroporation and radio frequency energy.

103. The method according to claim 78, wherein said energy administered is selected from the group consisting of ultrasound, heat, electroporation and radio frequency energy.

104. The method according to claim 90, wherein said energy administered is selected from the group consisting of ultrasound, heat, electroporation and radio frequency energy.